REMARKS

I. *Rejection of Claims Under 35 U.S.C. §102(b)*

The Examiner has rejected Claims 82, 84, 88, 89, and 97-100 under 35 U.S.C. §102(b) as anticipated by Vannier, *et al.* The Examiner has specifically requested that the Applicant, in order to make the Response to the previous Office Action (mailed January 17, 2001) fully responsive, address this rejection with respect to Claims 82, 84, 88, and 89.

Specifically, the Examiner states that Vannier, *et al.*, discloses:

> "...the expression of the extracellular domain of human follicle stimulating hormone receptor (hFSHR) in *E. coli* as a ubiquitin fusion protein, (see abstract). Vannier et al. also disclose that immunization of mice with said fusion protein (Ub-hFSHR) resulted in high affinity anti-receptor monoclonal antibodies. Immunization of monkeys with said fusion protein also induced the formation of anti-receptor antibodies (see page 13359 second paragraph, and page 1365, last paragraph). Consequently, the disclosure of Vannier et al. anticipates all the limitations of the instant claims."

With respect to Independent Claim 82, this rejection has been obviated by amendment of Claim 82 to more specifically recite the invention for which patent protection is sought. Amended Claim 82 now specifies a "ubiquitin fusion protein comprising ubiquitin fused to one or more epitope-containing segments at contiguous or non-contiguous locations within ubiquitin, wherein the epitope-containing segments comprising two or more identical or non-identical non-ubiquitin self-epitopes....". In contrast, Vannier, *et al.*, discloses a fusion protein comprising ubiquitin fused to amino acids 23-358 of FSHR, at the carboxyl-terminus (Ub-hFSHR(23-358). *See, e.g.*, page 1359, column 1, paragraph 5. The Vannier, *et al.*, fusion protein clearly does not meet the aforementioned limitations of: (*i*) the

epitope-containing segments being fused to ubiquitin at contiguous or non-contiguous locations within ubiquitin; and (*ii*) epitope-containing segments comprising two or more identical or non-identical non-ubiquitin self-epitopes. Therefore, amended Claim 82 is not anticipated by Vannier, *et al.*

Second, amended Claim 82 now recites that "the ubiquitin fusion protein is immunogenic for the non-ubiquitin self-epitopes contained therein...." In contrast, Vannier, *et al.*, discloses a fusion protein comprising ubiquitin fused to amino acids 23-358 of hFSHR which, when immunized into mice, results in the production of monoclonal antibodies that are immunogenic for hFSHR. However, Vannier, *et al.*, fails to disclose whether the epitopes within hFSHR were *self epitopes*, and whether this aforementioned immune response was generated to a *self-epitope*, as required by amended Claim 82. It should be noted that the FSHR in the ubiquitin-FSHR fusion protein disclosed by Vannier, *et al.*, was of human origin (rather than of murine or primate origin) and thus contained an abundance of non-self epitopes (*i.e.*, regions of amino acid sequence not conserved between humans and mice, or humans and monkeys). Accordingly, Vannier, *et al.*, fails to disclose use of a ubiquitin fusion protein to generate an immune response to a non-ubiquitin *self-antigen*.

Third, Claim 82 has been amended to expressly recite the limitation that the ubiquitin fusion protein comprises ubiquitin fused to an "epitope-containing segments comprising two or more identical or non-identical non-ubiquitin self-epitopes...." The identical epitopes of the present invention are indicated by the presence of repeating identical sequences of 10 or more amino acid residues, as illustrated, *e.g.*, on page 44, line 17-20, which refers to multiple copies of the GnRH epitope. Conversely, Vannier, *et al.*, teaches ubiquitin fused to amino acids 23-358 of FSHR, at the C-terminus. The presence of *multiple* epitopes within the FSHR sequences of the fusion protein disclosed by Vannier, *et al.*, is not analogous to the *identical* epitopes of

the present invention. Thus, there are no repeated sequences in the Vannier, *et al.*, FSHR fusion protein which would be understood to be *identical* epitopes by those of skill in the art.

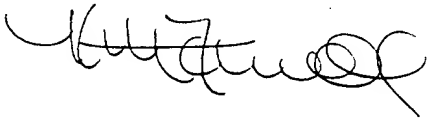
Claims 84, 88, and 89 are all dependent upon amended Claim 82. Moreover, Claim 88 has been amended to recite a "non-ubiquitin self-epitope..." Hence, for the reasons set forth above, these claims are not anticipated by Vannier, *et al.*

Therefore, in conclusion, Vannier, *et al.*, fails to anticipate Claims 82, 84, 88, and 89 under 35 U.S.C. §102(b).

Summary

In light of the above Amendments and Remarks, Applicants respectfully request reconsideration of the subject patent application.

Respectfully submitted,



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